Restriction Requirement and Election of Species

Claims 1-34 as originally filed were divided into two groups, group I, claims 1-32, and group II, claim 33, as summarized in the office action mailed June 14, 1994. Group I was elected and claim 33 cancelled.

Claims 1-5, 11-23, and 26-34 were determined to be generic, and a single species, initially a protein analog including SCRs from two different complement regulating proteins, which was changed to a protein analog having defined amino acid substitutions, was elected. Claims 1, 2, 6-9, 12-17, 21-24, and 27-34 were also determined to be generic and a single species, CR1, elected.

The withdrawal of the prior art rejections is greatly appreciated. Since all elected claims have now been found allowable over the prior art, consideration of the withdrawn claims directed to the non-elected species is earnestly requested.

Rejections under 37 C.F.R. §112

Claims 8, 9, 23 and 24 were rejected under 35 U.S.C. §112 as lacking antecedent basis and indefiniteness. These rejections are respectfully traversed if applied to the amended claims.

The claims have been amended into independent form and the withdrawn claims amended to correct their dependencies.

Double patenting rejection

Claim 9 was provisionally rejected under the doctrine of obviousness-type double patenting over claim 30 of now allowed U.S.S.N. 08/210,266, on the basis that the claimed changes herein at positions 114-121 are the same. This rejection is respectfully traversed. Additional changes to the sequence are required by claim 9 that are not disclosed in, nor obvious from, the changes defined by claim 30. These are more clearly shown as follows:

the amino acid sequence of human CR1 (Sequence ID No. 13) at 114-121 is: DNETPICD

claim 9 defines the sequences at 114-121 as:

109-112, 114-117, 121: STKPPICQ;

116: K(DNKTPICD); 116,117: K-P (DNKPPICD);

the remainder of the substitutions have been deleted:

114: D (DNETPICD); 115: N (DNETPICD); 121: D (DNETPICD); 117: T (DNETPICD)

Claim 30 defines the sequence at 114-121 as: DNETPICD.

Summary

Consideration on the merits and allowance of all claims 1, 3-5, 9-16, 18-20, 23-32 and 34 as pending is earnestly solicited. All claims as currently pending as amended upon entry

**Appendix**: Claims as pending after entry of amendment

1. (three times amended) An analog of a protein regulating complement activation having short consensus repeats of amino acid sequence selected from the group [of complement regulating proteins consisting] of complement receptor 1, complement receptor 2, decay accelerating factor, membrane cofactor protein, C4 binding protein, and factor H, and those complement regulating proteins wherein the carboxy terminus is removed to allow the protein to be secreted, wherein said protein analog is selected from the group consisting of complement regulating protein analogs containing short consensus repeats derived from a second, different complement regulating protein, complement regulating protein analogs wherein the short consensus repeats are rearranged, and complement regulating protein analogs consisting of as few as three short consensus repeats, wherein the protein analog binds C3b, C4b or C3b and C4b.

Please cancel claim 2.

3. (amended) The analog of claim [2] 1 wherein the protein is complement receptor one.

4. (amended) The analog of claim [2] 1 wherein the protein is decay accelerating factor.

5. (amended) The analog of claim [2] 1 wherein the protein is factor H.

8. (three times amended) [The] An analog of [claim 2] a protein regulating complement activation having short consensus repeats of amino acid sequence selected from the group consisting of complement receptor 1, complement receptor 2, decay accelerating factor, membrane cofactor protein, C4 binding protein, and factor H, and those complement regulating proteins wherein the carboxy terminus is removed to allow the protein to be secreted, wherein the protein contains a change within a short consensus repeat that corresponds with a change to complement receptor one as shown in Sequence ID No. 13 selected from the group consisting of:

CR1-4 with its first 122 amino acids (SCR1-2) (Sequence ID Nos 1 and 3) replaced with CR1 amino acids 497-618 (SCR 8-9) (Sequence ID Nos. 2 and 4) and CR1-4(8,9) with deletion of 194-253; and substitution of amino acids 271-543 with: T-R-T-T-F-H-L-G-R-K-C-S-T-A-V-S-P-A-T-T-S-E-G-L-R-L-C-A-A-H-P-R-E-T-G-A-L-Q-P-P-H-V-K (Sequence ID No. 11), or structurally similar amino acids.

9. (four times amended) [The] An analog of [claim 2] a protein regulating complement activation having short consensus repeats of amino acid sequence selected from the group consisting of complement receptor 1, complement receptor 2, decay accelerating factor, membrane cofactor protein, C4 binding

protein, and factor H, and those complement regulating proteins wherein the carboxy terminus is removed to allow the protein to be secreted, wherein the protein contains a change within a short consensus repeat that corresponds with a change to complement receptor one as shown in Sequence ID No. 13 selected from the group consisting of:
79: D (amino acid 19 of Sequence ID No. 4); 37,79: Y,D (amino acid 37 of Sequence ID No. 2 and amino acid 19 of Sequence ID No. 4); 92: T (amino acid 32 of Sequence ID No. 4); 109-112: N-A-A-H (amino acids 49-52 of Sequence ID No. 4); 109-112, 114-117, 121: N-A-A-H, S-T-K-P...Q (amino acids 49-52, 54-57, 61 of Sequence ID No. 4); 114-117, 121: S-T-K-P...Q; (amino acids 54-61 of Sequence ID No. 4) 116: K (amino acid 56 of Sequence ID No. 4); 116,117: K-P (amino acids 56-57 of Sequence ID No. 4); 92-94: K...Y (amino acids 32-34 of Sequence ID NO. 3); 99,103,106: S...T...I (amino acids 39, 43 and 46 of Sequence ID No. 3); 109-112: D-T-V-I (amino acids 49-52 of Sequence ID No. 3); 110: T (amino acid 50 of Sequence ID No. 3); 111: V (amino acid 51 of Sequence ID No. 3); 112: I (amino acid 52 of Sequence ID No. 3); [114: D (amino acid 54 of Sequence ID No. 3); 115: N (amino acid 55 of Sequence ID No. 3); 121: D (amino acid 61 of Sequence ID No. 3); 117: T (amino acid 57 of Sequence ID No. 3);] 1,3: Q...N (amino acids 1, 3 of Sequence ID No. 1); 6-9: E-W-L-P (amino acids 6-9 of Sequence ID No. 1); 12-16, 18-21: K-L-K-T-Q...N-A-S-D (amino acids 12-21 of Sequence ID No. 2); 27,29: S...K (amino acids 27,29 of Sequence ID No. 2); 37: S (amino acid 37 of Sequence ID No. 1); 44, 47, 49: I...K...S (amino acids 44, 47, 49 of Sequence ID No. 1); 52-54, 57, 59: T-G-A...R...R (amino acids 52-54, 57, 59 of Sequence ID No. 1); 78-79, 82: K-G...F (amino acids 18-19, 22 of Sequence ID No. 3); 85, 87: Q...K (amino acids 25, 27 of Sequence ID No. 3); 12-16, 18-21: R-P-T-N-L...D-E-F-E (amino acids 12-21 of Sequence ID No. 1); 27,29: Y...N (amino acids 27, 29 of Sequence ID No. 1); 35, 64-65, 94: G...R-N...Y (amino acid 35 of Sequence ID No. 1, amino acids 4-5, 34 of Sequence ID No. 3), substitutions with structurally similar amino acids, and combinations thereof.

10. (three times amended) [The] An analog of [claim 2 wherein the complement regulatory protein is] decay accelerating factor wherein one or more substitutions are introduced into the region of the protein corresponding to decay accelerating factor short consensus repeats SCRs 2-3 as shown in Sequence ID No. 17 selected from the group consisting of 180-187: S-T-K-P-P-I-C-Q (amino acids 54-61 of Sequence ID No. 4); 175-178: N-A-A-H (amino acids 49-52 of Sequence ID No. 4); 175-187: S-T-K-P-P-I-C-Q-N-A-A-H (Sequence ID No. 9); 130: R (amino acid 4 of Sequence ID No. 3); 145: D (amino acid 19 of Sequence ID No. 4); 77-84: K-L-K-T-Q-T-N-A-S-D (amino acids 12-21 of Sequence ID No. 2); 90-92: S-L-

K (amino acids 27-29 of Sequence ID No. 2), substitutions with structurally similar amino acids, and combinations thereof.

11. The analog of claim 1 wherein the complement regulatory protein is factor H comprising sequences conferring on the protein an activity selected from the group consisting of C3b binding activity, C3b cofactor activity, C4b binding activity, and C4b cofactor activity, wherein the sequences are derived from a protein selected from the group consisting of complement receptor 1, membrane cofactor protein, C4 binding protein, and factor H.

12. The analog of claim 1 comprising at least one short consensus repeat derived from a different protein selected from the group consisting of complement receptor 1, complement receptor 2, decay accelerating factor, membrane cofactor protein, C4 binding protein, and factor H.

13. (amended) The analog of claim 1 wherein the protein has C3b cofactor activity, C4b cofactor activity and decay accelerating activity.

14. (amended) The analog of claim 1 wherein the region of the protein having biological activity consists of three short consensus regions and has two complement regulatory activities.

15. The analog of claim 1 further comprising a pharmaceutically acceptable carrier for administration to a patient in need thereof.

16. (twice amended) A method for making an analog of a protein regulating complement activation having short consensus repeats of amino acid sequence selected from the group consisting of complement receptor 1, complement receptor 2, decay accelerating factor, membrane cofactor protein, C4 binding protein, and factor H, and these complement regulating proteins wherein the carboxy terminus is removed to allow the protein to be secreted, comprising

constructing a DNA sequence encoding a protein analog selected from the group consisting of complement regulating protein analogs containing short consensus repeats derived from a second, different complement regulating protein, complement regulating protein analogs wherein the short consensus repeats are rearranged, and complement regulating protein analogs consisting of as few as three short consensus repeats, wherein the protein analog binds C3b, C4b, or C3b and C4b, and

expressing the DNA sequence in a suitable host for expression of the protein.

Please cancel claim 17.

18. The method of claim 16 wherein the protein is complement receptor one.

19. The method of claim 16 wherein the protein is decay accelerating factor.

20. The method of claim 16 wherein the protein is factor H.

23. (three times amended) [The] A method [of claim 17] for making a protein regulating complement activation having short consensus repeats of amino acid sequence selected from the group consisting of complement receptor 1, complement receptor 2, decay accelerating factor, membrane cofactor protein, C4 binding protein, and factor H, and those complement regulating proteins wherein the carboxy terminus is removed to allow the protein to be secreted, wherein the protein analog [contains a change] is changed within a short consensus repeat [that corresponds with] to correspond to a change to complement receptor one as shown in Sequence ID No. 13 selected from the group consisting of:

CR1-4 with its first 122 amino acids (SCR1-2) (Sequence ID Nos. 1 and 3) replaced with CR1 amino acids 497-618 (SCR 8-9) (Sequence ID Nos. 2 and 4) and CR1-4(8,9) with deletion of 194-253; substitution of amino acids 271-543 with: T-R-T-T-F-H-L-G-R-K-C-S-T-A-V-S-P-A-T-T-S-E-G-L-R-L-C-A-A-H-P-R-E-T-G-A-L-Q-P-P-H-V-K (Sequence ID No. 11), or structurally similar amino acids.

24. (three times amended) [The] A method [of claim 17] for making a protein regulating complement activation having short consensus repeats of amino acid sequence selected from the group consisting of complement receptor 1, complement receptor 2, decay accelerating factor, membrane cofactor protein, C4 binding protein, and factor H, and those complement regulating proteins wherein the carboxy terminus is removed to allow the protein to be secreted, wherein the protein analog [contains a change] is changed within a short consensus repeat [that corresponds with] to correspond to a change to complement receptor one as shown in Sequence ID No. 13 selected from the group consisting of:
79: D (amino acid 19 of Sequence ID No. 4); 37,79: Y,D (amino acid 37 of Sequence ID No. 2 and amino acid 19 of Sequence ID No. 4); 92: T (amino acid 32 of Sequence ID No. 4); 109-112: N-A-A-H (amino acids 49-52 of Sequence ID No. 4); 109-112, 114-117, 121: N-A-A-H, S-T-K-P...Q (amino acids 49-52, 54-57, 61 of Sequence ID No. 4); 114-117, 121: S-T-K-P...Q; (amino acids 54-61 of Sequence ID No. 4) 116: K (amino acid 56 of Sequence ID No. 4); 116,117: K-P (amino acids 56-57 of Sequence ID No. 4); 92-94: K...Y (amino acids 32-34 of Sequence ID NO. 3); 99,103,106: S...T...I (amino acids 39, 43 and 46 of Sequence ID No. 3); 109-112: D-T-V-I (amino acids 49-52 of Sequence ID No. 3); 110: T (amino acid 50 of Sequence ID No. 3); 111: V (amino acid 51 of Sequence ID No. 3); 112: I (amino acid 52 of Sequence ID No. 3); [114: D (amino acid 54 of Sequence ID No. 3); 115: N (amino acid 55 of Sequence ID No. 3); 121: D (amino acid 61 of Sequence ID No. 3); 117: T

(amino acid 57 of Sequence ID No. 3);] 1,3: Q...N (amino acids 1, 3 of Sequence ID No. 1); 6-9: E-W-L-P (amino acids 6-9 of Sequence ID No. 1); 12-16, 18-21: K-L-K-T-Q...N-A-S-D (amino acids 12-21 of Sequence ID No. 2); 27,29: S...K (amino acids 27,29 of Sequence ID No. 2); 37: S (amino acid 37 of Sequence ID No. 1); 44, 47, 49: I...K...S (amino acids 44, 47, 49 of Sequence ID No. 1); 52-54, 57, 59: T-G-A...R...R (amino acids 52-54, 57, 59 of Sequence ID No. 1); 78-79, 82: K-G...F (amino acids 18-19, 22 of Sequence ID No. 3); 85, 87: Q...K (amino acids 25, 27 of Sequence ID No. 3); 12-16, 18-21: R-P-T-N-L...D-E-F-E (amino acids 12-21 of Sequence ID No. 1); 27,29: Y...N (amino acids 27, 29 of Sequence ID No. 1); 35, 64-65, 94: G...R-N...Y (amino acid 35 of Sequence ID No. 1, amino acids 4-5, 34 of Sequence ID No. 3), substitutions with structurally similar amino acids, and combinations thereof.

25. (three times amended) [The] A method [of claim 17 wherein the complement regulatory protein is] for making an analog of decay accelerating factor wherein one or more substitutions are introduced into the region of the protein corresponding to decay accelerating factor short consensus repeats SCRs 2-3 as shown in Sequence ID No. 17 selected from the group consisting of
180-187: S-T-K-P-P-I-C-Q (amino acids 54-61 of Sequence ID No. 4); 175-178: N-A-A-H (amino acids 49-52 of Sequence ID No. 4); 175-187: S-T-K-P-P-I-C-Q-N-A-A-H (Sequence ID No. 9); 130: R (amino acid 4 of Sequence ID No. 3); 145: D (amino acid 19 of Sequence ID No. 4); 77-84: K-L-K-T-Q-T-N-A-S-D (amino acids 12-21 of Sequence ID No. 2); 90-92: S-L-K (amino acids 27-29 of Sequence ID No. 2), substitutions with structurally similar amino acids, and combinations thereof.

27. (amended) The method of claim 16 comprising inserting into the protein analog at least one short consensus repeat derived from a different protein selected from the group consisting of complement receptor 1, complement receptor 2, decay accelerating factor, membrane cofactor protein, C4 binding protein, and factor H.

34. (twice amended) A method for enhancing the C4b or C3b cofactor activity of a complement regulatory protein, wherein the protein has either C3b or C4b cofactor activity, comprising adding sequences to the protein conferring binding of the other ligand, either C4b or C3b, wherein the sequences are present in a protein selected from the group of naturally occurring complement receptor 1, complement receptor 2, decay accelerating factor, membrane cofactor protein, C4 binding protein, and factor H.